REMARKS

Claims 14-22 are currently being examined. Applicants have amended claim 14 to more particularly and distinctly claim that which Applicants regard as their invention. No new matter has been introduced by this amendment.

I. Information Disclosure Statement

The Office has indicated that the crossed off references of the IDS submitted upon filing of this divisional application were missing from the parent application. Applicants submit the missing references for consideration by courier.

II. Double Patenting

Claims 14 -16 and 18-19 have been rejected under the doctrine of obviousness-type double patenting. Applicants agree to submit a Terminal Disclaimer and request that this submission be held in abeyance pending a final determination of the allowance.

III. Rejection Under 35 U.S.C. § 112, First Paragraph

A. Written Description

Claims 14-16 and 18-19 have been rejected as failing to comply with the written description requirement. The Office contends that the specification fails to provide adequate written description of the functional IFN-Fc variants. Applicants respectfully traverse this rejection.

Applicants again refer to the Guidelines referenced by the Examiner, specifically Example 14. In that example the conclusion was that variants were supported by the specification even though only a single species was disclosed because the functional language required functional activity of the variant and the specification provided an assay for function. The same is true here. Claim 14 as amended requires that the variant be functional and have 95% sequence identity with SEQ ID NO 1. Due to the routine nature of creating protein variants is routine in the art, the functional test is easily performed. The variants are limited to those that have 95% identity with SEQ ID NO 1. Therefore, Applicants submit that the Guidelines support a determination that the specification provides sufficient written description for the Genus of functional variants claimed and request that the rejection be withdrawn.

B. Enablement

Claims 14-16 and 18-19 have been rejected as lacking enablement. The Office contends that the state of the art is unpredictable and the Applicants have not provided sufficient guidance to produce the functional variants claimed. Applicants respectfully traverse this rejection.

As discussed in section A above, Applicants have claimed "functional variants" and have provided an assay to test such variants in Example II (4). The Office has already stated in the written description guidelines, Example 14, that the procedure for making protein variants such as substitutions, deletions, insertions etc. is conventional and routine, and NOT unpredictable as the Office presently contends. Applicants also assert that the viral assay provided is sufficient guidance to test such variants for functional activity. This testing is not undue, as the specification provides the necessary guidance to perform the assay, the techniques are routine for those skilled in the art, the level of skill in the art is high, there are working examples in the specification. It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *In re Wands,* 858 F.2d at 737, 740, 8 USPQ2d at 1404, 1407.

In view of all of these factors, Applicants submit that the specification provides an enabling disclosure for the entire breadth of the claimed functional variants, and request that the rejection be withdrawn.

IV. Rejection Under 35 U.S.C. § 103

Claims 14-16 and 18-19 have been rejected as unpatentable over Landolphi (U.S. Pat. No. 5,349,053), in view of Frincke (EP 467,416) or Peterhans Analytical Biochem). The Office contends that "it would have been prima facie obvious to one of ordinary skill in the art to substitute the interferon/Fc gamma chain fragment molecule of Landolphi with interferon alpha of Frincke to make a hybrid molecule that would be stable for in vivo use because of the recognized stability of hybrid as a preferred use as

set forth by Francke (sic)." (Office Action at page 12-13). Applicants respectfully traverse this rejection.

Although Applicants still contend that there is no motivation to combine the references as the Office contends, Applicants made a second argument as further evidence of nonobviousness. There are two ways to rebut the rejections, establish that the Office failed to meet its burden in establishing a prima facie case, or to present evidence of unexpected results. Applicants provided such evidence presented at page 6 (last paragraph) of the specification illustrating unexpected results. The Office did not address this argument in the present Office action. The *in vivo* pharmokinetic studies in primates resulted in a 40-fold longer serum half-life than unmodified interferon. The clearance half-life after subcutaneous injection was almost 120 fold longer. EP467416 only reported a 12-fold increase in half-life (col. 6, lines 53-57.) Since, the Landolphi patent only constructed IL-2-Ig complexes, and does not disclose any increases in half-life, the present invention clearly demonstrates unexpected results over this patent as well. Peterhans discloses labeled constructs labeled complexes for an entirely different purpose, thus no disclosure of increased half-life.

In view of the lack of a motivation to combine references, a lack of a reasonable expectation of success, and the unexpected results presented in the present disclosure, the § 103(a) rejection should be withdrawn.

Conclusion

In view of the previous remarks, Applicants submit that the claims are in condition for allowance and request rejoinder of claims 17, 20-22.

Respectfully Submitted

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